IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF ILLINOIS

IN RE: TESTOSTERONE REPLACEMENT THERAPY PRODUCTS LIABILITY LITIGATION	MDL No. 2545 Master Docket Case No. 1:14-cv-01748 Honorable Matthew F. Kennelly
This document applies to: *Brad Martin, et al. v. Actavis, Inc., et al.,* Case No. 15-cv-4292 *Casey Brubaker, et al. v. Actavis, Inc., et al.,* Case No. 15-cv-426	

PLAINTIFFS' MEMORANDUM OF LAW IN OPPOSITION TO ACTAVIS DEFENDANTS' MOTION FOR SUMMARY JUDGMENT BASED ON FEDERAL PREEMPTION

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I. INTRODUCTION

This Court has already denied on several occasions the preemption defenses of both AbbVie and Auxilium and held that design-defect claims are not preempted and that it was not impossible for those defendants to strengthen their products' labels consistent with their parallel federal and state law duties. Nevertheless, Defendants Actavis, Inc., Actavis Pharma, Inc., and Actavis Laboratories UT, Inc. (hereinafter "Defendants" or "Actavis") contend that their motion should meet a different fate.

Actavis' preemption argument relating to Plaintiffs' design-defect claim has already been rejected by this court, as discussed *infra*, since Plaintiffs do not allege that Actavis needed to change the design of Androderm. Next, Actavis erroneously contends that they could not unilaterally change their label because they are prohibited from changing the Highlights section of their label without prior FDA approval. Actavis' argument does not stand up to scrutiny as Plaintiffs' position is only that additional warnings should have been added to the label in general, not that the Highlights section of the label needed to be changed. While Plaintiffs would certainly have welcomed a change to the Highlights section of the label, Defendants could have unilaterally updated the Full Prescribing Information section of their label and then sought FDA approval to make those same changes to the Highlights section.

Defendants also argue that there was no "newly-acquired" information available to support a change to their label under the "changes-being-effected" ("CBE") regulation. As discussed below, sufficient information existed between the time Actavis submitted its New Drug Application for Androderm and the time Plaintiffs suffered their injuries such that Actavis was not only able, but obliged, to implement stronger cardiovascular ("CV") warnings under the CBE regulation. Because Actavis was never precluded from adding additional warnings to its label, none of Plaintiffs' claims are preempted. Lastly, Actavis' argument that claims of off-label promotion be preempted has also been rejected by this court because Plaintiffs' off-label claims do not seek to enforce the Federal Food, Drug, and Cosmetic Act ("FDCA").

II. LEGAL STANDARD

On a motion for summary judgment, "[t]he moving party bears the burden of establishing that there is no genuine issue of material fact and that it is entitled to judgment as a matter of law." *Esdale v. Am. Cmty. Mut. Ins. Co.*, 914 F. Supp. 270, 271 (N.D. Ill. 1996). At summary judgment, the underlying facts are reviewed in the light most favorable to the nonmoving party. *Harley-Davidson Motor Co. v. PowerSports, Inc.*, 319 F.3d 973, 989 (7th Cir. 2003). "'The choice between reasonable inferences from facts' is a function of a fact-finder, and when multiple reasonable inferences exist on a genuine issue of material fact, summary judgment will not be appropriate." *Id.*

III. ARGUMENT

A. Plaintiffs' Design Defect Claims Are Not Preempted Because Plaintiffs Do Not Seek to Alter Androderm's Design

Actavis moves to dismiss Plaintiffs' design defect claims as being preempted even though this argument was rejected in CMO 76, when Auxilium presented the same defense. *See* CMO 76. Conveniently, Actavis seems to ignore this Court's ruling on this very issue. Like Auxilium before it, Actavis argues that, under *Mutual Pharm. Co. v. Bartlett*, 133 S. Ct. 2466 (2013, and *Yates v. Ortho-McNeil-Janssen Pharms., Inc.,* 808 F.3d 281 (6th Cir. 2015), Plaintiffs' design-defect claims are preempted. Actavis argues that because the FDA approved the formulation of Androderm, they were precluded from offering a different design for the product. *Bartlett* and *Yates* are inapplicable here, however, because Androderm was approved by the FDA *only for use in men with classic hypogonadism*.

Whether or not the design of Androderm is defective when used by men with classic, true hypogonadism, the product is defectively designed for use in men with age-related declines in their testosterone and/or symptoms of aging with which Defendants sought to associate such declines. This is so because there is no evidence that Androderm is effective in treating the symptoms for which Defendants promoted the product. When used in this fashion, Androderm has absolutely no utility – there is simply no reason to believe it works. With no countervailing benefit, any risks are unacceptable, even if the risks of the drug might have been outweighed by some benefits in men who suffer from classical hypogonadism. Because Androderm increases the risk of major cardiovascular

and venous thrombotic events, it is defectively designed for treatment of age-related declines in serum testosterone because it exposes men using it for that purpose to risks without any countervailing benefits.

Indeed, Androderm may be worse than useless in such men. As set forth in the expert report of Dr. Hossein Ardehali, low serum testosterone may be the result of other age-related conditions, including obesity, type 2 diabetes, and metabolic syndrome. *See* Plaintiffs' Expert Hossein Ardehali General Causation Report at 38-39, attached as Exhibit 1. Aging men with these conditions are already at risk for major cardiovascular events. *See id.* at 8-11. Because Androderm can increase the risk of such events, its use may be particularly pernicious in men whose low testosterone levels are a marker that they are already at an increased risk for the same adverse health events. These patients—the very patients to whom Actavis marketed Androderm—are precisely the men who should *not* use Androderm. In short, for men who were prescribed Androderm and did not suffer from actual primary or secondary hypogonadism, Androderm was necessarily defective in its design and it should have never been sold as a product to treat age-related hypogonadism. *See* General Report of Peggy Pence, PhD, RAC, FRAPS, dated February 5, 2018, (hereinafter "Pence Report") attached as Exhibit 2 at 147. This conclusion is in no way at odds with the FDA's approval of the product, because the FDA never approved Androderm for this use.

Plaintiffs thus do not argue, and do not need to argue, that Actavis never should have started, or should have stopped, selling Androderm because of its defective design, a theory of liability that some courts have rejected. *See Yates*, 808 F.3d at 300; *but see Young v. Bristol-Myers Squibb Co.*, No. 4:16-CV-00108-DMB-JMV, 2017 U.S. Dist. LEXIS 24730, at *21 (N.D. Miss. Feb. 22, 2017) (stop selling doctrine does not preclude a pre-approval theory of recovery); *Guidry v. Janssen Pharms., Inc.,* 206 F. Supp. 3d 1187 (E.D. La. 2016) ([T]the raison d'être of products liability litigation is to penalize manufacturers who design unreasonably dangerous products in hopes that they never start selling them. State products liability law functions as a compliment to federal drug regulations to keep unreasonably dangerous drugs off the market.). Plaintiffs argue instead that Actavis never should have started, or should have stopped, marketing Androderm for age-related hypogonadism, low serum

testosterone levels, and the general symptomology of aging because Androderm is defectively-designed when used for those conditions. Actavis thus did not need to re-formulate Androderm; it needed to stop marketing Androderm for conditions for which its design was inherently defective.

This theory is in no way at odds with the FDA's approval of Androderm for use in men with classic hypogonadism nor would Actavis have been in violation of any federal law obligations had it ceased promoting Androderm for the off-label uses to which it was sold. This Court should adhere to its ruling in CMO 76 and find that "because [Plaintiff] does not seek to alter [Androderm's] design, his claim is not precluded under *Bartlett* or *Yates*." CMO 76.

B. Plaintiffs Failure to Warn Claims are Not Preempted

1. Actavis Could Independently Change the Androderm Package Insert Without Changing the Highlights Section of the Androderm Label

Defendants mischaracterize Plaintiffs' failure-to-warn theory in order to advance their legally and factually unsupported argument. The crux of Defendants' argument is the unfounded statement that Plaintiffs' failure-to-warn claims are premised on the position that the Androderm labeling in effect prior to Plaintiffs' first prescriptions should have included the same warning language the FDA approved for addition to the Androderm labeling in May 2015. *See* Memorandum in Support of Actavis' Motion for Summary Judgment on Federal Preemption (hereinafter "Defs' Memo") at p. 8. Defendants claim that because the May 2015 label change included a change to the Highlights section of the label, they would have been unable to make that change unilaterally prior to Plaintiffs' first prescriptions because such a change requires FDA approval. *Id.* This argument must fail because Plaintiffs' failure-to-warn claim *is not* premised on the theory that Actavis needed to have added the exact same, May 2015, warning language to the Highlights section of the Androderm label at an earlier time.

In Plaintiffs' Fourth Amended Complaint, Plaintiffs have generally pled that "Defendants knew or should have known that the product created significant risks of serious bodily harm to consumers, and they failed to adequately warn consumers and/or their health care providers of such risks." *See* Fourth Amended Master Long Form Complaint at ¶ 479. Nowhere in the Complaint do

Plaintiffs' allege that the May 2015 warnings that were added to Androderm's label should have been implemented at an earlier time nor do Plaintiffs plead that changes should have specifically been made to the Highlights section of the Androderm label.

Plaintiffs' regulatory expert, Peggy Pence, opines in her report that there were a variety of warnings that Defendants should have added to their label. *See* Pence Report, Ex. 2 at 145-46. While the suggested warnings are similar to the added warnings in the May 2015 label, nowhere in her report does she state that the exact warnings added to the May 2015 label needed to be added earlier nor does she state that changes needed to be made to the Highlights section of the label. *See id.* Instead, at her deposition, Pence stated that "similar" warnings to those added in May 2015 should have been added to the label prior to Plaintiffs' first prescriptions of Androderm. *See* April 5, 2018 Deposition of Peggy Pence at 173:16, 190:14-15, 191:15, 194:1-24, 195:2, 195:9, attached as Exhibit 3.

In sum, Plaintiffs' failure-to-warn claims have never been premised on the need to change the Highlights section of the Androderm label. Just because Defendants' did eventually add additional warnings to the Androderm label in May 2015, including changes to the Highlights section of the label, does not mean that any proposed changes to the label by the Plaintiffs also would have needed to be added to the Highlights section. If this were the standard, the entire CBE scheme of allowing drug manufacturers to unilaterally change their label upon learning "newly acquired information" would be upended. Defendants could have made unilateral changes to the Full Prescribing Information at some point prior to Plaintiffs' injuries and first prescriptions and then could have subsequently sought FDA approval to amend the highlights section of the label.

Additionally, 21 C.F.R. § 201.57(a)(1) makes clear that the Highlights section of the label does not need to include all the information contained in the Full Prescribing Information section of a drug's label:

> Highlights limitation statement. The verbatim statement "These highlights do not include all the information needed to use (insert name of drug product) safely and effectively. See full prescribing information for (insert name of drug product).

As Plaintiffs' failure-to-warn claims have never been premised on the need for the exact changes that were made to the Highlights section of Androderm's label in May 2015, Defendants could have added some or all of the changes that Plaintiffs proposed to the Full Prescribing Information section of the Androderm label without changing the Highlights section. Accordingly, Plaintiffs' claims cannot be preempted on this basis.

2. Plaintiffs Have Identified Newly Acquired Information That Would Support a Label Change

Yet again, Actavis has turned a blind eye to this Court's prior rulings and rehashes the same arguments that this Court has previously rejected. The difference here is that Actavis tries to move the goal posts, without any legal support, to claim that in order to unilaterally change a label, "newly acquired information[1]" must have been acquired at some point between the last label change prior to Plaintiffs' being prescribed Androderm, which occurred on April 26, 2012, and Plaintiffs' first prescriptions of Androderm in October 2012 and December 2013. This is in stark contrast to the actual requirement which is that new information must be acquired after product approval (not after the last label iteration prior to an injury). *See Utts v. Bristol-Myers Squibb Co.*, 251 F. Supp. 3d 644, 662–63 (S.D.N.Y. 2017) ("The 'newly acquired information,' **which is information that was not submitted to the FDA prior to the FDA's approval of the drug and its label**, must reveal risks of a 'different type or greater severity or frequency than previously included in submissions to [the] FDA.' 21 C.F.R. § 314.3(b).") (emphasis added).

The Defendants make this argument in an effort to differentiate their argument from those arguments made by the other defendants in this litigation, however, Defendants argument must fail because they provide no legal support for their contention. In fact, in the cases cited to by Defendants, the question is whether newly acquired information came out after *product approval*, not after the last label change prior to a plaintiff's injury. *See e.g. Mitchell v. Boehringer Ingelheim Pharm., Inc.*, No.

[1] "'Newly acquired information' is not limited to new data, but also encompasses 'new analyses of previously submitted data.'" *See Wyeth v. Levine*, 555 U.S. 555, 568 (2009) (citing 73 Fed. Reg. 49604. "The rule accounts for the fact that risk information accumulates over time and that the same data may take on a different meaning in light of subsequent developments. . . ." *See id.*

116CV02384STAEGB, 2017 WL 5617473 (W.D. Tenn. Nov. 21, 2017) ("The Court finds that Plaintiff has sufficiently pled that newly acquired information, **i.e., information acquired after Jardiance was approved by the FDA** on August 1, 2014 . . . .") (emphasis added). Indeed, "newly acquired information" is defined as "data, analyses, or other information not previously submitted to the Agency. . . ." 21 C.F.R. § 314.3. Thus, the newly acquired information must only be "acquired" after product approval, which would be after September 29, 1995, the day the initial New Drug Application ("NDA") for Androderm was approved. *See* Pence Report, Ex. 2 at 72.

While April 26, 2012 does mark the date that a label for a new strength of Androderm was approved under a Supplemental New Drug Application ("sNDA"), Defendant cites to no caselaw holding that new information must be acquired after the approval of an sNDA, when the same drug, albeit a different strength, has already been on the market. Additionally, *Mason v. SmithKline Beecham Corp* makes clear the FDA's failure to require additional warnings, in the context of approving other label changes, does not amount to clear evidence the FDA would have rejected those additional warnings if they had been proposed by the manufacturer. *See Mason v. SmithKline Beecham Corp.,* 596 F.3d 387, 395 (7th Cir. 2010).

As discussed *supra*, the true question is whether any newly acquired information that would support a label change came out between the initial approval of Androderm (1995) and Plaintiffs' first prescriptions of Androderm (2012 and 2013). In its previous decisions addressing and rejecting Defendants' preemption arguments, this Court has recognized that drug "manufacturers are not limited to the warning approved by the FDA but may unilaterally add additional warnings [through the CBE regulations] – and thereby comply with state-law duties under failure to warn – without violating federal requirements." CMO 47 at *7, citing 21 C.F.R. §314.70(c)(6)(iii). As the Court in *Wyeth* explained, the CBE regulation "accounts for the fact that risk information accumulates over time and that the same data may take on a different meaning in light of subsequent developments." *Wyeth,* 555 U.S. at 569. Under the regulation, as quoted in the Supreme Court's opinion, if a manufacturer "'conducts a new analysis of data showing risks of a different type or of a greater severity

or frequency than did reports previously submitted to FDA, the sponsor meets the requirement for 'newly acquired information.'" *Id.*

Because federal law requires a manufacturer to maintain responsibility for its label at all times, and further allows a manufacturer to update its label in view of newly acquired risk information – the same updates required by state law – federal law generally does not preempt state warning law in cases involving brand-name prescription drugs. A rare exception applies when a manufacturer can prove with clear evidence that, before the plaintiff was prescribed the drug in question, the FDA would have taken the necessary steps to rescind a CBE labeling change to add the warning required by state law. *Id.* at 571. In *Mensing,* the Supreme Court confirmed that federal law preempts a state-law duty to warn only where there is "clear evidence" that the FDA would have "rescinded" a CBE labeling change to add the warning required by state law. *PLIVA, Inc. v. Mensing,* 564 U.S. 604, 635 n.8 (2011)

In concluding that it was not impossible to have strengthened their TRT labels post-approval in compliance with CBE regulations, this Court previously rejected similar arguments made by AbbVie and Auxilium. *See* CMO 47 and 76. The fact of the matter is that copious amounts of new information justifying a stronger warning was acquired by Actavis between the approval of Androderm and Plaintiffs' first prescriptions of the drug[2].

Ten years prior to Plaintiffs' first prescriptions of Androderm, members of the men's health and urologic medical communities began raising questions about testosterone's safety and efficacy and

[2] Defendants' argue that this new information must have been acquired prior to the Plaintiffs' first prescriptions in October 2012 and December 2013. However, Mr. Brubaker did not suffer his heart attack until March 4, 2014. Prior to his injury, in November 2013 and January 2014, two studies finding an association between TRT and cardiovascular risks (Vigen 2013, and Finkle 2014) finally spurred FDA intervention, at which time the it released the January 31, 2014 safety announcement informing the public that it was investigating the risk of strokes, heart attack, and death in men taking FDA-approved testosterone products. If changes were made to the Androderm label prior to Mr. Brubaker's heart attack occurring, but after his first prescription, Mr. Brubaker still could have heeded those new warnings and stopped use of Androderm prior to suffering his heart attack. Since Actavis cites to no caselaw requiring that the new information be acquired prior to the first prescription, as opposed to an injury occurring, these studies alone constitute newly acquired information supporting a label change prior to Mr. Brubaker's injuries. Therefore, Actavis' preemption argument must fail as to Mr. Brubaker on this basis alone.

implored the manufacturers to conduct adequate testing. In 2002, a group of doctors began calling on TRT companies to conduct further studies because "no studies to date have included a sufficient number of participants to adequately" assess the risk/benefit ratio of testosterone given the larger-than-expected population of users. *See* Pence Report, Ex. 2 at 87-88 (citing Asthana S, Bhasin S, Butler R, et al. Maculine Vitality: Pros and Cons of Testosterone in Treating the Andropause. *J Gerontol*, 2004; 59A(5):461-465).[3] Moreover, the authors acknowledged the need for a large prospective randomized, placebo-controlled trial with approximately 6,000 participants which had been made by a consortium of academic andrologists.

In November 2002, the National Institute on Aging ("NIA") announced a task force led by the Institute of Medicine ("IOM") to investigate, review, and assess the current state of knowledge concerning testosterone replacement therapy. *See* Pence Report, Ex. 2 at 89. The IOM released a report of its findings in 2004. Plaintiffs' regulatory expert, Peggy Pence, has opined that the release of the 2004 IOM report should have provided Defendants with sufficient information to update its label:

> The IOM report put the Androderm Defendants and other companies marketing and selling testosterone products on notice regarding a safety signal of off-label use in aging men. There is a known high prevalence of diseases such as diabetes, obesity, cardiovascular disease and metabolic syndrome in the aging male population which are associated with elevated risk of major cardiovascular events. Therefore, there was also a signal to the Androderm Defendants that men at high risk for cardiovascular events were being exposed to testosterone products.

See Pence Report, Ex. 2 at 93.

In 2004, the *Journal of the American Medical Association* published a letter to the editor from the Director of FDA Division of Reproductive and Urologic Drug Products ("DRUP") stating that, despite the 50 year history of using testosterone, "no randomized controlled studies have been conducted to support the widespread use of testosterone in men for [male climacteric] condition, and the adverse-event profile of the drug in this population has not been studied adequately." *See* Pence

[3] The authors also invoked a comparison between TRT and HRT (hormone replacement therapy) for women, to make the point that further HRT testing had been necessary in order to establish that the drug increased – rather than decreased – cardiovascular and breast cancer risks.

Report, Ex. 2 at 75-76. (citing Shames D. Risk of Testosterone Replacement. *New Engl J Med* 2004; 350(19):2004-2006).

In 2007, FDA officials responded to the recent publication of the Endocrine Society's Clinical Practice Guideline on testosterone therapy in adult men and stated "the Patient Guide, however, fails to include any clear warnings to patients regarding the more serious adverse outcomes that could result from testosterone therapy, such as prostate cancer or cardiovascular events . . . ." *See* Pence Report, Ex. 2 at 77 (citing Shames D, Gassman A, Handelsman H. COMMENTARY: Guideline for Male Testosterone Therapy: A Regulatory Perspective. J Clin Endocrinol Metab February 2007;92(2):414-415.)

The growing fear that testosterone replacement therapies were being marketed to a much larger audience than that for which they were indicated without adequate testing of the attendant risks finally led to the Testosterone in Older Men ("TOM") Study. TOM was funded by the National Institute on Aging of the NHI, and in 2009 had to be prematurely terminated due to an observation of a much higher rate of cardiovascular events in the testosterone-arm of the trial versus the placebo–arm (23 to 5). *See* Plaintiffs' Expert Burt Gerstman's Report (hereinafter "Gerstman Report") dated February 5, 2018, at 15, 84-86 attached as Exhibit 4. Fortunately, the data from TOM was preserved and the results were eventually published in a 2010 study. *See* Basaria S, Coviello AD, Travison TG, Storer TW, Farwell WR, Jette AM, et al. (2010), *Adverse Events Associated with Testosterone Administration*, New England Journal of Medicine, 363(2), 109-22. The TOM study ultimately led to the FDA issuing a Tracked Safety Issue (TSI) for testosterone products. *See* Gerstman Report, Ex. 4 at 15.

In May 2010, FDA's Division of Epidemiology ("DEPI") submitted the results of its review of two meta-analyses and one systematic qualitative review which it was asked to review and comment on by FDA's DRUP after being notified of the discontinuation of TOM trial. *See* Pence Report, Ex. 2 at 139. Defendants cite to selective portions of DEPI's report, *see* Defs' Br. at 11, but while the report did not find conclusive evidence of a causal connection one way or the other, the report stated that "[u]pon review of these articles the DEPI reviewer observed that the studies highlight some trends that could represent signals of unknown effects of TRT in certain age and disease groups of

treated men. The observed trends include a possible increased risk of cardiovascular events . . . ." *Id.* at p.140.

In 2011, the NIA advised that "[a]dditional information on safety of testosterone administration is needed because, although several small short-term clinical trials have been conducted in older men, these studies do not provide adequate information to assess the safety of testosterone as used in clinical practice." *See* Pence Report, Ex. 2 at 94 (citing NIA, NIH FOA, Release Date July 28, 2011, Expiration Date November 3, 2011: Analysis of Databases from Health Care Systems or Large Epidemiologic Studies to Evaluate Safety of Testosterone Administration in Older Men (R01)). "Moreover, adequate information on safety is lacking in regard to many important adverse outcomes, particularly in regard to long-term testosterone use." *Id.*

Even after the unmistakable notice established by the abrupt cancellation of the TOM study and the clear calls for further testing by the NIA and other experts in the field, there was still no attempt made by Actavis or its predecessors to change the Androderm label to warn of the suspected CV risks.

Not only did Actavis know of testosterone's propensity to cause cardiovascular events, it also knew that Androderm had not been adequately tested to determine its safety. Generally, "[a] manufacturer ... [has] the duty to perform reasonable tests and inspections to discover latent hazards." *Sparks v. Oxy-Health, LLC*, 134 F. Supp. 3d 961, 992 (E.D.N.C. 2015); *see also Block v. Woo Young Medical Co. Ltd.,* 937 F.Supp.2d 1028, 1039 (D. Minn. March 28, 2013) ("there was sufficient evidence of a risk of cartilage damage to alert Woo Young to the possible need for warnings and to the potential need for more testing to determine the safety of its pain pump"); *Monroe v. Zimmer U.S. Inc.*, 766 F. Supp. 2d 1012 (E.D. Cal. 2011) (the expert testimony and evidence suggested a viable "duty to test" that should be brought to the jury); *Creech v. Stryker Corp.,* No. 2:07CV22 DAK, 2012 WL 33360, at *3 (D. Utah Jan. 6, 2012) (rejecting Stryker's attempt to dismiss plaintiff's claim that Stryker negligently failed to test its pumps).

Ultimately, once the FDA learned what Actavis has known – or at the very least, suspected – all along, a change to the labeling of Androderm to add CV risks was mandated in 2015. In 2015, the label was changed to include the previously unmentioned risk of myocardial infarction and stroke:

> 5.5 Cardiovascular Risk
>
> Long term clinical safety trials have not been conducted to assess the cardiovascular outcomes of testosterone replacement therapy in men. To date, epidemiologic studies and randomized controlled trials have been inconclusive for determining the risk of major adverse cardiovascular events (MACE), such as non-fatal myocardial infarction, non-fatal stroke, and cardiovascular stroke, with the use of testosterone compared to non-use. Some studies, but not all, have reported an increased risk of MACE in association with use of testosterone replacement therapy in men. Patients should be informed of this possible risk when deciding whether to use or to continue sue of AndroGel 1%.

See Pence Report, Ex. 2 at 96 (quoting AndroGel 1% Labeling, 2015). These warnings and calls for further testing were old hat to Actavis at this point. Testing of Androderm should have been commenced a decade or more ago, and the manufactures of Androderm should have fulfilled their duty to their consumers and conveyed the warning of CV events long before any of the Plaintiffs were made to suffer those injuries.

All of the information described above could not have been known to the FDA at the time of Androderm's approval of the initial label in 1995, and therefore clearly constitutes newly acquired information, the likes of which permitted this Court to reject earlier preemption defenses:

> In a previous ruling, the Court determined that there was no "clear evidence" that the FDA would have rejected efforts by AbbVie to add warnings about cardiovascular risk to the AndroGel warning labels. *See In re: TRT*, 2017 WL 1836435, at *7–*11. The regulatory history for Testim is similar to that of AbbVie, and Auxilium has not offered any new facts or cited any changes in the law that would warrant reconsideration of the Court's previous ruling.

CMO 76 at *10. Plainly, the law has not materially changed since CMO 76. Nevertheless, Actavis suggests that the same arguments previously rejected by this Court should now be accepted. However, Actavis is unable to meet the demanding burden for its affirmative defense, nor have they met their burden to have this Court reconsider its prior rulings.

Actavis' also makes another previously denied argument relating to the 2014 Public Citizen Petition. Actavis argues the FDA's finding that "there is insufficient evidence of a causal link between testosterone therapy and adverse cardiovascular outcomes" in response to the 2014 Public Citizen Petition establishes that "there was (and is not) reasonable evidence of a causal association and the requirements for adding a warning utilizing CBE are not met." *See* Defs' Br. at 13. When this Court rejected AbbVie's argument regarding the same petition, it concluded: (1) the FDA did not state definitively that TRT is not causally associated with cardiovascular risk, but rather that it wanted to conduct its own evaluation of the matter, including the 2014 Advisory Committee; and (2) the FDA responded only to a specific request for label change, one not made by the pharmaceutical company. CMO 46 at *10-11. The Court concluded that "because there are other explanations for the FDA's rejection of the Citizen's Petition, this rejection does not constitute clear evidence that the FDA would have rejected an attempt by AbbVie to add the warnings that plaintiffs contend were wrongfully omitted." *Id.* at *11. Accordingly, Defendants' motion should be denied.

C. Plaintiffs' Off-Label Promotion Claims Do Not Impermissibly Seek to Enforce the FDCA and are Not Preempted

Plaintiffs' off-label promotion claims that are based on Defendants' conduct in promoting TRT label expansion do not constitute an impermissible attempt to bring a private cause of action under the FDCA, as this Court has previously held in ruling on AbbVie's identical motion. *See* CMO 47 at *7-8. While the FDCA bars off-label marketing of drugs by their manufacturers, it creates no private cause of action for violations of its provisions. *See Blinn v. Smith & Nephew Richards, Inc.*, 55 F. Supp. 2d 1353, 1361 (M.D. Fla. 1999). A private plaintiff may, however, assert a state law tort claim that is based in part on a defendant's conduct that happens to occur in violation of the FDCA. *See* CMO 47 at *7-9*; In re Neurontin Mktg. & Sale Practices Litig.*, 244 F.R.D. 89, 92 n.6 (D. Mass. 2007); *Hosler v Alcon Labs., Inc.*, 2012 U.S. Dist. LEXIS 145176, *35, 2012 WL 4792983 (S.D. Fla. Oct. 9, 2012). Simply because conduct violates the FDCA does not mean that a state law claim based on the same conduct depends on the FDCA's existence. *Lefaivre v. KV Pharm. Co.*, 636 F.3d 935, 944 (8th Cir. 2011).

The question, then, is how to determine whether a claim formally asserted under state law is in substance one seeking to enforce the FDCA. The Supreme Court supplied the test in *Buckman*. If the claim would not exist in the absence of the FDCA, it is impliedly preempted. *Buckman v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 353 (2001). In other words:

> [T]he conduct on which the claim is premised must be the type of conduct that would traditionally give rise to liability under state law—and that would give rise to liability under state law even if the FDCA had never been enacted. If the defendant's conduct is not of this type, then the plaintiff is effectively suing for a violation of the FDCA (no matter how the plaintiff labels the claim), and the plaintiff's claim is thus impliedly preempted under Buckman.

Riley v. Cordis Corp., 625 F. Supp. 2d 769, 777 (D. Minn. 2009). In *Buckman*, for example, the Court deemed preempted a state tort claim that the defendant defrauded the FDA in the course of obtaining approval for its medical devices and that, as a result, the devices improperly obtained market clearance and were later used to the plaintiffs' detriment. The claims, the Court held, did not rely on "traditional state tort law which had predated" the FDCA, for the Act's existence was "a critical element" of the plaintiffs' case. 531 U.S. at 353. In other words, were it not for the federal regulatory scheme the FDCA created, there would have been no fraud that could support the tort claim. *Loreto v. P&G*, 515 Fed. Appx. 576, 579, 2013 U.S. App. LEXIS 3813, *5-6 (6th Cir. Ohio 2013).

As this Court has previously held, Plaintiffs' claims arising out of off-label promotion do not depend on the existence of the FDCA or even whether Defendants conduct violates the FDCA[4]:

> In the present cases, plaintiffs' marketing claims are not impliedly preempted by the FDCA or under *Buckman*, because the claims are grounded in traditional state law principles of liability, such as negligence, failure to warn, strict product liability, and fraud that predate the relevant FDCA requirements. The claims do not depend on violations of requirements or prohibitions imposed by the FDCA.
>
> ***
>
> As plaintiffs contend and as the Court has noted, plaintiffs' off-label claims do not depend on a finding that AbbVie violated the FDCA or FDA regulations. For example, a reasonable jury could find AbbVie liable for making misrepresentations

[4] Defendants only argue that Plaintiffs' off-label claims are preempted. They do not make any argument as to the sufficiency of evidence that Plaintiff has presented relating to Defendants' off-label marketing.

> about the safety and efficacy of AndroGel for treating age-related hypogonadism or for making misrepresentations about the indications for which the FDA approved AndroGel. And although plaintiffs' complaints make reference to regulations regarding misbranding, they do so in the context of establishing the standard of care that they contend AbbVie breached, and to help establish AbbVie's intent and motive in connection with its marketing of AndroGel. *See, e.g.*, Fourth Am. Master Compl. ¶¶ 494-500. The fact that plaintiffs cannot assert claims to enforce the FDCA's prohibitions or requirements does not preclude them from, for example, introducing evidence regarding the indications for which the FDA approved AndroGel. "Buckman does not mean plaintiffs cannot bring state law claims based on conduct that violates the FDCA." *Eidson v. Medtronic, Inc.*, 981 F. Supp. 2d 868, 880-81 (N.D. Cal. 2013).

CMO 46 at *7-9. Even where Plaintiffs allege conduct that does also violate the FDCA, their claims do not arise from or depend on that violation. It is the falsity of Actavis' statements, not the violation of federal law, that gives rise to these claims. Accordingly, Plaintiffs' off-label promotion claims are not preempted.

IV. CONCLUSION

In light of the above, Actavis' motion for summary judgment on the ground that Plaintiffs' failure-to-warn and design-defect claims are preempted should be denied in its entirety.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on June 8, 2018, I electronically transmitted the foregoing document to the Clerk of the United States District Court using the CM/ECF system for filing and service to all parties/counsel registered to received copies in this case.

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